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## Mucolytic treatment with N-acetylcysteine L-lysinate metered dose inhaler in dogs: airway epithelial function changes.

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N-acetylcysteine L-lysinate Nacystelyn (L-NAC) is a newly synthesized mucolytic agent, of which the action *in vivo* has not been well defined. In six healthy male dogs, the rheological properties of mucus, its mucociliary and cough clearability, and the transepithelial potential difference (PD) of the tracheobronchial epithelium were evaluated after placebo and L-NAC metered dose inhaler (MDI) aerosols. The principal index of mucus rigidity, log G\*, decreased at all airway sites with L-NAC administration, i.e. the mucus became less rigid and more deformable (the overall change in G\* was 0.29 log units, i.e. ca. twofold decrease). The viscoelasticity-derived mucus transportability parameters, mucociliary (MCI) and cough (CC) clearability indices, increased with L-NAC MDI, particularly CCI, which probably reflects the effect of mucus rheology on cough clearability. PD increased significantly with L-NAC administration at all measurement sites, which appears to be a novel effect of this direct acting mucolytic agent. Tracheal mucus linear velocity (TMV) increased with L-NAC compared with placebo, as did the normalized frog palate transport rate (NFPTR). The increase in NFPTR was greater than that predicted from the mucus rheological properties alone, suggesting that L-NAC still resident in the colloid mucus stimulated the frog palate cilia. The index of mucus flux, the collection rate mg·min<sup>-1</sup>, was higher with L-NAC compared with placebo. From our results we conclude that L-NAC shows potential benefit in terms of improving mucus rheological properties and clearability. It may act, in part, by stimulating the secretion of mucus of lower viscoelasticity. The stimulation of mucociliary clearance could be related to ion flux changes, as indicated by the increase in PD.

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